RESEARCH PRODUCT CATALOG

Enzo Diagnostics

To Our Customers

Since its establishment in 1976, Enzo has developed expertise in the chemical modification of nucleic acids. In 1982 Enzo introduced the first of its ***BioProbe***® Systems for the nonradioactive labeling and detection of nucleic acids. Throughout the years, following a program of development and innovation, we have expanded our product line and introduced new products to meet the ever-expanding needs of the research community. This vast experience in nucleic acid probe technology is available to the researcher in this new, easy-to-use product catalog.

Enzo Diagnostics offers a full range of products designed for use in the scientific research community. For nucleic acid labeling Enzo has gone beyond its original biotin label and now offers a wide choice of proprietary labeled nucleotides expanded to include a complete line of digoxigenin- and fluorescent-modified nucleotides. These nucleotides are now offered in newly formatted, easy-to-use modular systems allowing the researcher to produce high quality nonradioactive nucleic acid probes by such procedures as nick translation, terminal labeling, random priming, RNA labeling and our unique ***OligoBridge***™ labeling system. Detection reagents include our highly versatile and sensitive ***DETEK***® Signal Generating Systems for rapid, colorimetric detection in both *in situ* and membrane hybridization procedures.

Our ***MaxSense***™ Membrane Hybridization and Detection Systems offer the scientist all the reagents required for nonradioactive Southern, Northern or dot blot analyses. For those interested in *in situ* hybridizations, Enzo has been a pioneer and leader in the field for many years and we have developed complete systems for both *in situ* hybridization and detection.

The Enzo Microplate Hybridization Assay System, an easy-to-use, rapid and nonradioactive method for detecting DNA in a microtiter well, represents an exciting new generation of DNA probe technology. Kits are currently available for detection of HIV, *Mycobacterium tuberculosis* complex and both Hepatitis B core antigen and surface antigen.

Enzo's labeling and detection systems have been designed for both the experienced molecular biologist and the first-time user. We pride ourselves on the quality of our products and the quality of our service.

We hope you will call us with your comments and ideas for new products so that we can better serve you. Our technical service representatives are available to help you.

Terms and Conditions

Shipped via: **Domestic:** Federal Express, Standard Service (Priority, if specified)
International: Please inquire

In stock items: Orders received by noon will be processed and shipped out the same day. All others, next day shipment.

Backorder items: Will be advised at time of ordering.

Shipping charges: F.O.B. Farmingdale, New York

Terms: Net 30 Days

Claims: Shipping damages or shortages must be made within five (5) business days of receipt of order and accompanied by a written statement.
Permission to return products will not be given without prior authorization from Enzo Diagnostics, Inc.
Products must be returned within five (5) days of receipt of order.

Research Use Only

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Limited Warranty

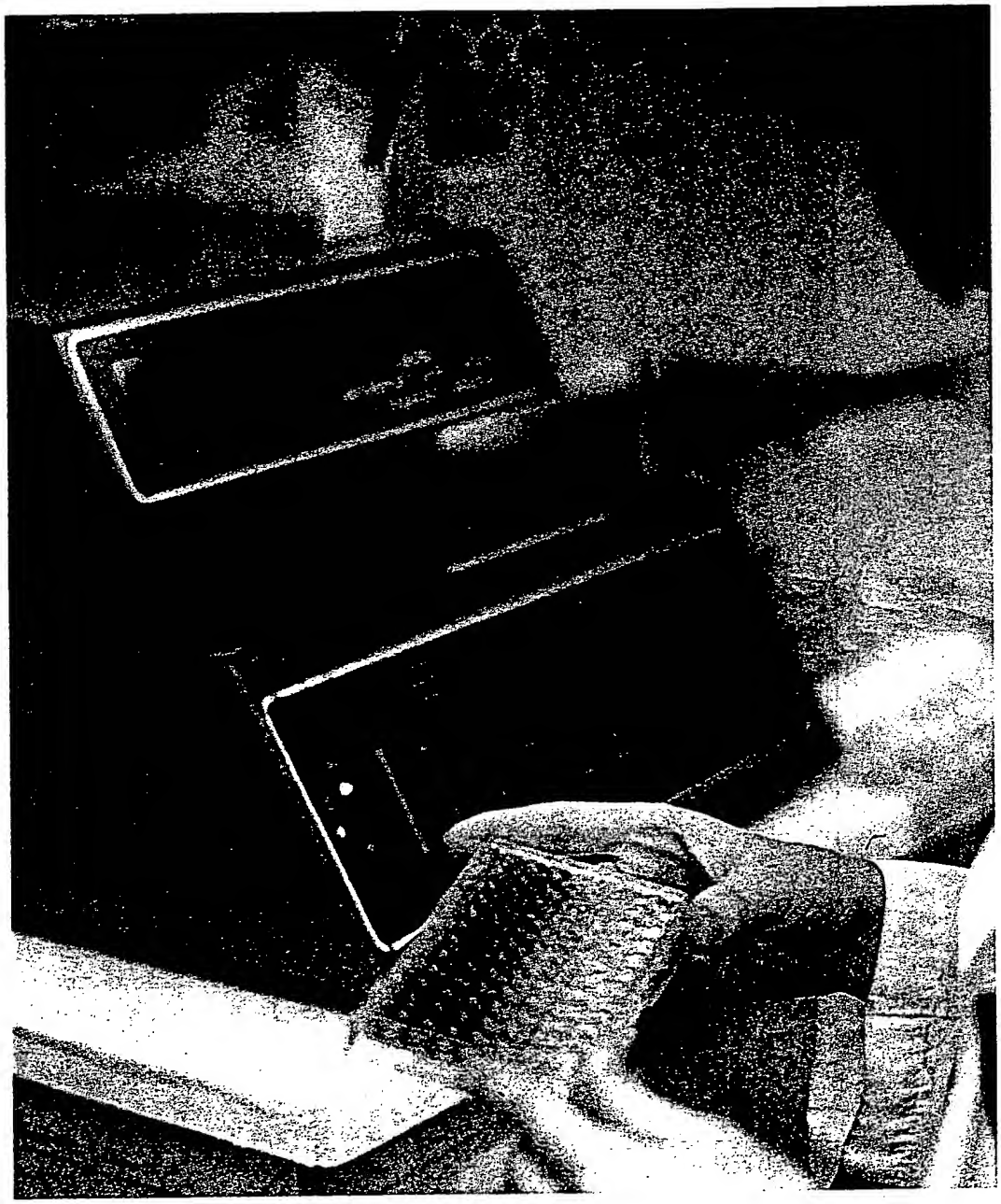
These products are offered under a limited warranty. The products are guaranteed to meet all appropriate specifications described in the package insert at the time of shipment. Enzo Diagnostics' sole obligation is to replace the product to the extent of the purchase price. All claims must be made to Enzo Diagnostics, Inc. within five (5) days of receipt of order.

Prices and Shipping Charges Subject to Change Without Notice.

Inquiries for volume discounts are welcome.

Contents

Microplate Hybridization Assays



Enzo
The Source for
Microplate Hybridization Assays

The Targets:

- *HIV 1*
- *M. tuberculosis*
- *HIV 2*
- *Hepatitis B Virus (core antigen sequences)*
- *Hepatitis B Virus (surface antigen sequences)*
- *Hepatitis B Virus (direct detection in serum)*

The Companions:

- SK38 and SK39
- MTB10 and MTB11
- VB306 and VB310
- HB01 and HB02
- HB07 and HB08
- HB012 and HB014
- HB011 and HB013
- HBV Titration Standards

♦ Quantify standard and non-standard amplification procedures

♦ If you need a number, we have a microplate assay for you

• Well Done!

Enzo originated and developed the first microtiter well hybridization and detection assays. Similar microplate hybridization systems have proliferated as the ease and utility of the format has become more appreciated.

• Take a Number, Please

In addition to being quick and reproducible, the microplate hybridization assay format is quantitative. Because the spectrophotometric readout of the results of the microplate hybridizations can be used to generate standard curves, the colorimetric assay results are quantifiable. Instead of just the presence or absence of color, you can get a number–without radiolabel!

• Specific Detection following Amplification

Most of the Enzo Microplate Hybridization Assays are designed for detection and quantitation of specific sequences of nucleic acid produced by either *in vitro* or *in vivo* sequence amplification. The method provides greater sensitivity than some radiolabeling techniques and it offers an additional level of assurance by positively identifying the target sequence of interest.

• Infectious Agents, a Primary Target

The organisms that are detected by the Enzo Microplate Hybridization Assays include infectious agents of great concern in health care in today's society: HIV 1, HIV 2, *Mycobacterium tuberculosis* and hepatitis B virus. Enzo also provides a specially formatted microplate assay for the direct detection and quantitation of hepatitis B DNA in serum specimens. The assay can be used as a tool for monitoring the status of an hepatitis B infection and the efficacy of various therapies.

Microplate Hybridization Assays*

- ***Rapid***
- ***Reproducible***
- ***Quantitative***

Enzo is the innovator of microplate-based hybridization assays. The impetus for the development of this innovative method came from the fact that the colorimetric, nonradioactive hybridization assays that became possible with the advent of hapten-modified nucleotides lacked the quantifiable nature of radiolabeling of nucleic acid probes. In addition, when nonradioactive labeling of nucleic acids and nonradioactive hybridization and detection was a science in its infancy, antibody-antigen ELISA assays were quickly becoming important tools in the clinical laboratory as well as research in virology, immunology, pathology, epidemiology and other areas. The union of these two fields, nonradioactive nucleic acid probing studies and the ELISA format, was the force behind the development of these assays.

The use of the microplate format assays for quantitative analyses of nonradioactive probes was first reported by Cook, *et al.* (1988). It was demonstrated that hapten labels contained on deoxynucleotides "outside" the region of hybridization were more effective than were hapten labels contained "within". Such fine differences in the signaling efficacy of nonradioactive labeling strategies were not detectable by non-quantitative techiques.

Adding to these historical aspects of the development of the microplate hybridization format was another, now obvious, concept–target amplification makes almost any nucleic acid target level accessible to any detection technique. An important aspect of this concept, of course, is that the detection technique MUST be sufficiently stringent to compensate for potential promiscuity of the amplification technique. Furthermore, promiscuous aspects of any amplification technique are exacerbated by the amount of amplification required to generate a sufficient amount of target sequence to achieve detection. At Enzo, we have addressed these concerns to provide the optimum microplate assays.

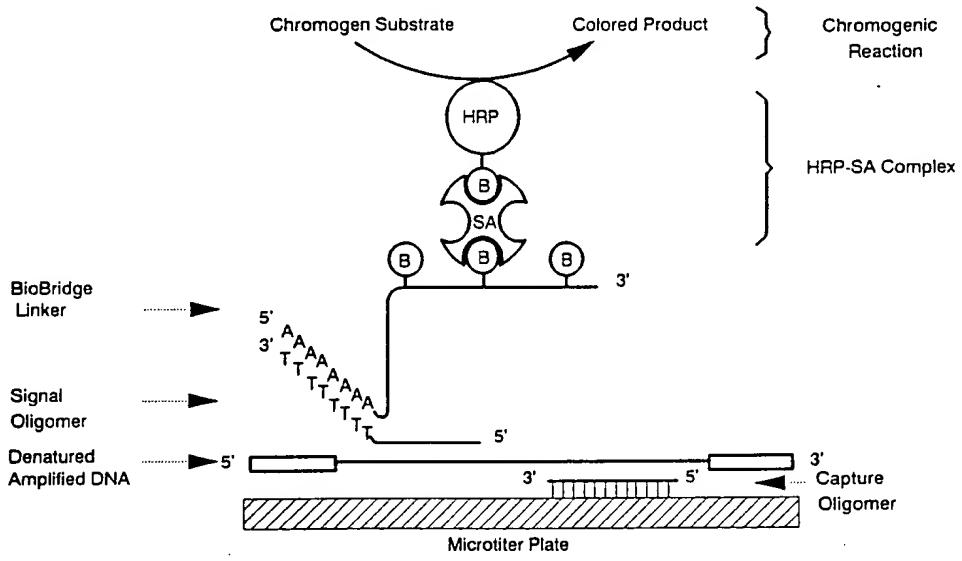
Microplate Hybridization Assay (MHA)

Principles

The principle of the **Enzo Microplate Hybridization Assay** format is shown below. In the assay, a target nucleic acid is first hybridized to a well-bound capture probe. It is then detected in a series of steps involving hybridization with a second, signal probe. Unique to the Enzo Microplate Hybridization Assays, the signal probe does not contain a hapten label, but is labeled with a T-tail. The signal probe, which is bound to the microplate through the target nucleic acid, is hybridized to the Enzo *BioBridge*® Linker labeling molecule. This serves to deliver a signal strength that is unattainable by direct labeling of the signal probe with biotin, making Enzo's microplate hybridization assays extremely sensitive to low target levels. The bound *BioBridge*® Linker is then bound by *DETEK*® Hrp and the complex is allowed to react with chromogen and substrate for color development. The results of the assay can be interpreted by eye when only a yes/no result is required. By use of a microplate or microstrip reader, the results can be quantitated by spectrophotometry.

Figure 1

Schematic Representation of the Enzo Microplate Hybridization Assay



All of the microplate hybridization assays are carried out in the same fashion. The assays require 3 hours and all of the procedures are performed at room temperature.

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Microplate Hybridization Assay

Performance Characteristics

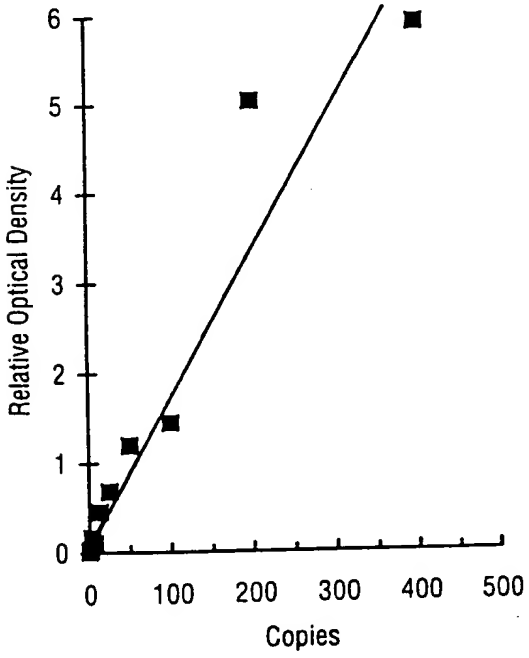
The utility of the microplate format was well illustrated by its use in the detection of HIV 1 in white blood cell preparations [Rapier, J. M., *et al.* (1993)]. These studies demonstrated the utility and strength of the microplate assay format as a whole, in addition to demonstrating the format's utility in the study of HIV infection, prognosis and treatment. Some of the unique aspects of the **Enzo Microplate Hybridization Assays** make it the most useful system for the study of rare nucleic acid sequences. In fact, the principle and the technique are applicable to any nucleic acid sequence of interest for which quantitation is desirable.

All of the standard **Microplate Hybridization Assays** are performed in an identical manner. In fact, several different targets can be analyzed in the same assay run provided the individual capture wells and the specific signal probes are used. Thus, a researcher interested in both HIV 1 and HIV 2 sequences in a sample of amplified material could run both assays at one time using two sets of capture strips and the two signal probes.

Although each of the **Enzo Microplate Hybridization Assays** is designed for the detection of a specific target organism and a specific sequence, the uniformity and consistency of the assays, in addition to the universal principle behind the assays, make the performance characteristics identical for all of the standard assays. Specifically, each of the assays requires approximately 10^7 to 10^8 copies of target DNA to generate a positive response. In situations in which *in vitro* target amplification techniques are used, as in a study of HIV 1 by Rapier, J. M., *et al.* target levels as low as 2-5 copies are detectable. In this assay, human DNA was seeded with varying amounts of HIV 1 DNA. The HIV 1 sequences were amplified using HIV 1-specific primers. The amplified DNA was then detected with the Microplate Hybridization Assay for HIV 1. The results, Figure 2, illustrate the remarkable linearity of response of the assay to the mock samples.

Figure 2

Analytic Sensitivity*



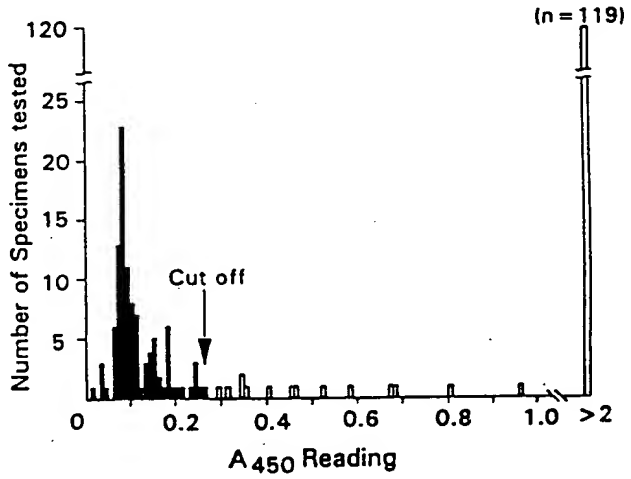
Sample Number	Copies	Relative A_{450}
2393	8×10^5	93.45
2410	8×10^4	38.28
2398	8×10^3	15.38
2391	800	8.74
2390	400	5.91
2395	200	5.03
2400	100	1.44
2394	50	1.19
2403	25	0.682
2397	12.5	0.455
2399	6.25	0.104
2402	3.12	0.170
2392	1.56	0.038
2396	0	0.014
water	0	0.003

*For details see Rapier, J. M., *et al.* (1993).

The reproducibility, consistency and quantitative aspects of the assay allowed the determination of the presence of HIV 1 DNA in white cells of patient blood specimens. Rapier, J. M., *et al.* showed that when over 100 seronegative and over 140 seropositive individuals' blood were examined, a clear cut distinction between the seropositive and seronegative population could be made. Averaging the results from the seronegative individuals, a cut off value was established as the average plus 3 standard deviation units. All but one of the seropositive sera were found to yield results that exceeded the cut off value. These results are illustrated in Figure 3.

Figure 3

Clear Cut-off Point



Samples from positive and negative specimens plotted to demonstrate the clear negative cut off obtained with the assay.

In studies using the **Microplate Hybridization Assay for HBV**, a similar correlation was found [Brakel, C. L. (1994), unpublished observations]. In that assay, sera were examined by serology for evidence of HBV infection. Surface antigen negative sera were used to generate a similarly determined positive-negative cut off. Sera that were entirely free of evidence of HBV infection generated microplate results that were lower than the cut off value. The only sera yielding results that exceeded the cut-off were sera with serological evidence of HBV infection. These results confirm the utility of the microplate hybridization assay format for the examination of specimens for rare nucleic acid sequences.

Microplate Hybridization Assays (MHA)

Each kit contains all of the required reagents, including a positive control so that the user can easily monitor the success of each assay run. Thus, in a simple procedure, one can determine the presence or absence of a specific nucleic acid sequence in up to 96 samples in less than 4 hours of work.

All kits include

Denaturation Reagent, 3 ml
Dilute alkaline solution containing indicator

Hybridization Buffer, 10 ml
Buffered sodium chloride/EDTA containing formamide and hybridization enhancers

Signal Probe, 6 ml
Organism-specific probe modified with a T-tail in buffered sodium chloride/EDTA containing formamide, hybridization enhancers and indicator

Linker, 6 ml
Modified poly-dA in buffered sodium chloride/sodium citrate containing detergent

20X Rinse Buffer, 25 ml
Buffered sodium chloride/sodium citrate containing detergent

10X Detection Reagent, 1 ml
Streptavidin-horseradish peroxidase complex in buffered sodium chloride, stabilizer and detergent

Detection Buffer, 10 ml
Buffered sodium chloride/EDTA containing stabilizer and detergent

Chromogen Reagent, 1.5 ml
5 mg/ml tetramethylbenzidine (TMB) in solvent

Reaction Buffer/Substrate Reagent, 15 ml
Dilute hydrogen peroxide in citrate phosphate buffer

Stop Solution, 12 ml
Dilute acid solution

Positive Control, 0.1 ml
Organism-specific DNA

Precoated Microwells, 96 wells
Microwell strips (six 2 x 8 doublet strips in a strip holder) coated with organism-specific capture probe

Plate Sealer, 2
Plastic seal for covering microwells for storage and for use during the assay runs

MHA

Ordering Information

The **Standard Microplate Hybridization Assays** are available for the following:

The MHA for HIV 1 provides materials for the colorimetric detection of nucleic acid containing HIV 1 *gag*-specific sequences.

The MHA for *M. tuberculosis* DNA provides materials for the colorimetric detection of nucleic acid containing proprietary sequences specific for the *M. tuberculosis* complex, which includes *M. africanum, M. bovis, M. tuberculosis* and *M. microti*. The isolation and characterization of the specific probe was detailed by Picken, R. N., *et al.* (1988).

The MHA for HBV core antigen DNA provides materials for the colorimetric detection of nucleic acid containing core antigen-specific sequences. The use of this region for determination of the presence of HBV DNA was described by Monjardino, J., *et al.* (1991).

The MHA for HIV 2 DNA provides materials for the colorimetric detection of nucleic acid containing HIV 2 *gag*-specific sequences.

The MHA for HBV surface antigen DNA provides materials for the colorimetric detection of nucleic acid containing surface antigen-specific sequences. The use of this region for determination of the presence of HBV DNA has been described by Yokosuka,O., *et al.* (1993).

HIV 1	Cat. No. 46330
Mycobacterium tuberculosis	Cat. No. 46340
HBV (core antigen)	Cat. No. 46350
HIV 2	Cat. No. 46360
HBV (surface antigen)	Cat. No. 46380

Microplate Hybridization Assay Companion Products

- ***Oligonucleotide Pairs***
- ***Target-Specific Probes***
- ***Target Amplification***

To assist the researcher in use of the **Enzo Microplate Hybridization Assays** and to provide target-specific oligonucleotide probes, Enzo provides several companion products. The products consist of oligonucleotide pairs that are chosen to be up- and down-stream of the nucleic acid sequence target of the particular microplate hybridization assay.

The oligonucleotide pairs could be used as target specific probes when terminal labeled with Terminal Deoxynucleotide Transferase as described in **Section 1, Nonradioactive Labeling of Nucleic Acids.**

Alternatively, using a template-dependent polymerase and a nucleotide mixture containing a hapten-modified nucleotide, the oligonucleotides might be used to generate labeled target-specific nucleic acid sequences by primer extension in both *in vitro* and *in situ* labeling reactions.

Each of the oligonucleotides is delivered in water at a concentration of 25μM. For some of the target nucleic acid sequences of interest, two different oligonucleotide pairs are available, allowing mixing and matching of the pairs for use in various target detection procedures.

Oligonucleotide Pairs

25 µM, 5 nanomoles each

The oligonucleotides SK38 and SK39 are complementary to unique, conserved sequences in the *gag* gene of HIV 1. They were first used as reported by Ou, C-Y., *et al.* (1988).

The oligonucleotides MTB10 and MTB11 are complementary to the unique, proprietary sequences of the Enzo probe for the *M. tuberculosis* complex (see Picken, R. N., *et al.*, 1988).

The oligonucleotides HB01 and HB02 are complementary to conserved sequences in the core antigen gene of HBV DNA. These specific sequences were obtained from the HBV genomic sequence reported by Fujiyama, A., *et al.* (1983).

The oligonucleotides HB07 and HB08 are complementary to unique, conserved sequences in the core antigen gene of HBV DNA. These specific sequences were obtained from the HBV genomic sequence reported by Fujiyama, A., *et al.* (1983). Similar sequences were also used by Monjardino, J., *et al.* (1991).

The oligonucleotides HB011 and HB014 are complementary to unique, conserved sequences in the surface antigen gene of HBV DNA. The specific sequences were obtained from the HBV genomic sequence reported by Fujiyama, A., *et al.* (1983) and the report of Yokosuka, O., *et al.* (1983).

The oligonucleotides HB012 and HB013 are complementary to sequences in the surface antigen gene of HBV DNA. The specific sequences were obtained from the HBV genomic sequence reported by Fujiyama, A., *et al.* and the report of Yokosuka, O., *et al.* (1993).

The oligonucleotides VB306 and VB310 are complementary to unique, conserved sequences in the *gag* gene of HIV 2. They were used and reported originally by Rayfield, M., *et al.* (1988).

SK38 and SK39 *Complementary to HIV 1*	Cat. No. 46331
MTB10 and MTB11 *Complementary to Mycobacteria tuberculosis*	Cat. No. 46341
HB01 and HB02 *Complementary to Hepatitis B (core antigen)*	Cat. No. 46351
HB07 and HB08 *Complementary to Hepatitis B (core antigen)*	Cat. No. 46355
HB011 and HB014 *Complementary to Hepatitis B (surface antigen)*	Cat. No. 46381
HB012 and HB013 *Complementary to Hepatitis B (surface antigen)*	Cat. No. 46382
VB306 and VB310 *Complementary to HIV 2*	Cat. No. 46361

Enhanced Microplate Hybridization Assay (EMHA) for Hepatitis B DNA

Principles

Viral hepatitis caused by hepatitis B virus is a major health care problem in many areas of the world. A blood-borne agent that is readily transmitted, hepatitis B virus is also considered a sexually-transmitted viral agent. The outcome of an infection by hepatitis B virus can be monitored by the progressive appearance and disappearance of viral antigens and the appearance of antibodies against major viral antigens. However, as a prognostic indicator of the resolution of infection and an indicator of the effect of various therapies currently under development, a useful determinant of the health status of a hepatitis patient is the level of HBV DNA in the serum. In addition to providing a tool for monitoring the progress of the infection and the efficacy of a therapeutic regimen, the detection of viral DNA in serum can be indicative of the infectious state of a patient and an indication of possible re-activation of virus.

Enzo has developed a simple, easy-to-use, nonradioactive format for assaying the HBV DNA in serum specimens. The **Enhanced Microplate Hybridization Assay (EMHA) for Hepatitis B DNA**, provided as a complete kit for use on human serum specimens, contains all required assay materials including materials for the preparation and pretreatment of the serum samples. In studies conducted by Enzo scientists and by independent laboratories, the **Enzo Enhanced Microplate Hybridization Assay for Hepatitis B DNA** performed with a sensitivity of detection that matched a radioactive assay in use in many clinical laboratories. A comparison, by an independent laboratory, of the results of the two assay formats is illustrated in Figure 4 (page 111). The data illustrate the accuracy of the assay and demonstrate its equivalence to a radioactive assay.

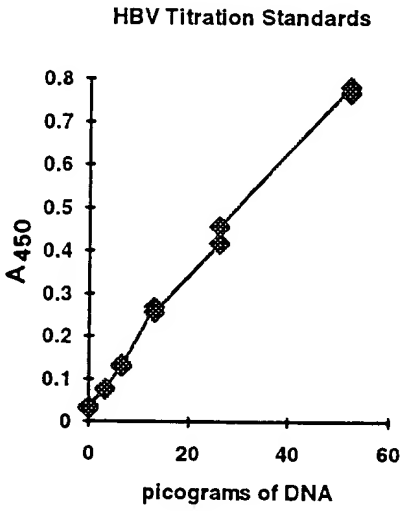
Comparison of Enhanced Microplate Assay with Radiolabel Assay

In this comparison, the **Enhanced Microplate Hybridization Assay for Hepatitis B DNA Serum Specimen Titration Standards** were used to generate a standard curve for determination of HBV DNA in serum specimens. From the standard curve, the amount of HBV DNA in 14 patient specimens was calculated by interpolation. The results of the EMHA were then compared to results obtained using a standard radiolabel assay for hepatitis B DNA, results of which are also reported as picograms of HBV DNA.

Figure 4

Detection of Hepatitis B DNA by the Enhanced Microplate Hybridization Assay (EMHA) for Hepatitis B DNA and a Radiolabel Assay for Hepatitis B DNA

Sample	Picograms of DNA	EMHA A_{450}
Neg. Std.	0	0.030
Neg. Std.	0	0.036
Standard E	3.25	0.077
Standard E	3.25	0.075
Standard D	6.5	0.134
Standard D	6.5	0.130
Standard C	13	0.268
Standard C	13	0.256
Standard B	26	0.418
Standard B	26	0.457
Standard A	52	0.782
Standard A	52	0.768



Sample	EMHA Result (picograms)	Radiolabel Assay (picograms)
1	48	43.9
2	10	9.2
3	0	0
4	> 100	156.2
5	0	0
6	0	0
7	22.5	25.5
8	0	0
9	> 100	148.6
10	0	0
11	0	0
12	0	0
13	1	0
14	0	0

The data show that the two assays are directly comparable, yielding identical results for the tested specimens.

The sensitivity of the EMHA for hepatitis B DNA is approximately 20 to 80 times that of a standard microplate assay. The additional sensitivity is achieved as a result of the use of more than one capture probe and several signal probes in additon to the use of a high performance detection reagent. With the EMHA for hepatitis B DNA, one can test and quantify the amount of HBV DNA in 48 duplicate specimens in 4 to 5 hours. The results are as reliable and as sensitive as those obtained with a radiolabel assay requiring overnight incubation and considerably more "hands on" time to process 25 specimens.

The procedure for use of the Enhanced Microplate Hybridization Assay (EMHA) for hepatitis B DNA is very similar to that of the standard microplate assays. The major differences are related to the pretreatment of the serum specimens. The specimen must be treated to release and denature the viral DNA prior to addition to a special hybridization solution in the capture wells. The procedure is completely detailed in the package insert and is very easy to understand and perform.

The procedure recommends the use of duplicate wells for assaying the serum specimens. The result of the procedure is identical in most respects to that for the standard Microplate Hybridization Assays (MHA) as illustrated in Figure 1, except that the detection reagent for the Enhanced Microplate Hybridization Assay (EMHA) is a high performance detection reagent as indicated in the detailed list of the assay.

Enhanced Microplate Hybridization Assay (EMHA) for Hepatitis B DNA

Kit includes

Sample Digestion Reagent, 8 ml
Acidified aqueous detergent solution with pH indicator

NaOH Denaturant, 4 ml
3N NaOH

RS Hybridization Buffer, 10 ml
Buffered NaCl/EDTA containing formamide and hybridization enhancers

HBV Signal Probe Mix, 6 ml
Modified hepatitis B-specific probes in buffered NaCl/EDTA containing formamide, hybridization enhancers and indicator

Linker, 6 ml
Modified poly-dA in buffered sodium chloride/sodium citrate containing detergent

20X Rinse Buffer, 25 ml
Buffered sodium chloride/sodium citrate containing detergent

10X HP Detection Reagent, 1 ml
Streptavidin-horseradish peroxidase conjugate in buffered NaCl, stabilizer and detergent

Detection Buffer, 10 ml
Buffered NaCl/EDTA containing stabilizer and detergent

Chromogen Reagent, 1.5 ml
5 mg/ml tetramethylbenzidine (TMB) in solvent

Reaction Buffer/Substrate Reagent, 15 ml
Dilute hydrogen peroxide in citrate phosphate buffer

Hepatitis B Positive Control, 0.5 ml
Pretreated plasmid DNA carrying HBV DNA sequences

HBV DNA Preparation Control, 0.5 ml
Plasmid DNA carrying HBV DNA sequences in heat inactivated calf serum

Stop Solution, 12 ml
Dilute acid solution

Precoated Microwells, 96 wells
Microwell strips (Six 2 X 8 doublet strips in a strip holder) coated with hepatitis B-specific capture probe

Plate Sealer, 2
Plastic seal for covering microwells for storage and for use during the assay runs

Enhanced MHA for HBV	Cat. No. 46353

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Serum Titration Standards

The standards include hepatitis B sequences in amounts to provide linear assay results between 3 and 50 picograms. The standard curve generated by these samples can be used to quantify the amount of hepatitis B DNA in serum specimens (see Figure 4).

Kit includes

HBV Negative Serum, 1 ml

HBV Standards A-E, 0.5 ml each
Heat inactivated bovine serum containing EDTA, preservative and decreasing amounts of hepatitis B recombinant plasmid DNA

Serum Titration Standards	Cat. No. 46354

SECTION SUMMARY

Microplate Hybridization Assays

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MTB Microplate Hybridization Assay	46340
Oligonucleotide Pair (MTB10 and MTB11)	46341
HBV (*core antigen*) Microplate Hybridization Assay	46350
Oligonucleotide Pair (HB01 and HB02)	46351
Oligonucleotide Pair (HB07 and HB08)	46355
HIV 2 Microplate Hybridization Assay	46360
Oligonucleotide Pair (VB306 and VB310)	46361
HBV (*surface antigen*) Microplate Hybridization Assay	46380
Oligonucleotide Pair (HB011 and HB014)	46381
Oligonucleotide Pair (HB012 and HB013)	46382
Enhanced Microplate Hybridization Assay (EMHA) for Hepatitis B DNA	46353
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MICROPLATE HYBRIDIZATION ASSAYS

SECTION 7 — Page No.

MONOCLONAL ANTIBODIES FOR IMMUNOPATHOLOGY

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APPLICANT: JANNIS G. STAVRIANOPOULOS ET AL.

TITLE: COMPOSITION EMPLOYING CHEMICALLY LABELED OLIGONUCLEOTIDE OR POLYNUCLEOTIDE, AND KIT AND APPARATUS CONTAINING SAME

☒ Express Mail Label No. EF436871773

☐ First Class Mailing Date

DATE MAILED: OCTOBER 5, 1995

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- ☐ Declaration
- ☐ Drawings
- ☐ Assignment
- ☐ Response to OA
- ☒ Amendment (PRELIMINARY)
- ☐ Issue Fee
- ☒ Other (see below)

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